<u>WHAT IS CLAIMED IS:</u>

1.   A method for reducing pain in a subject in need thereof by increasing ion flow through KCNQ potassium channels in a cell, the method comprising the step of administering to the subject a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound able to increase ion flow through KCNQ potassium channels, said composition administered to the subject in a potassium channel-opening amount, thereby reducing pain in the subject.

2.   The method of claim 1, wherein the pain is somatic pain.

3.   The method of claim 2, wherein the pain is cutaneous.

4.   The method of claim 2, wherein the pain is visceral.

5.   The method of claim 2, wherein the pain is caused by a burn, a bruise, an abrasion, a laceration, a broken bone, a torn ligament, a torn tendon, a torn muscle, a viral infection, a bacterial infection, a protozoal infection, a fungal infection, contact dermatitis, inflammation, or cancer.

6.   The method of claim 5, wherein the inflammation is caused by trauma, infection, surgery, burns, or diseases with an inflammatory component.

7.   The method of claim 1, wherein the pain is neuropathic.

8.   The method of claim 7, wherein the neuropathic pain is caused by injury to the central or peripheral nervous system due to cancer, HIV infection, tissue trauma, infection, autoimmune disease, diabetes, arthritis, diabetic neuropathy, trigeminal neuralgia or drug administration.

9.   The method of claim 1, wherein the subject is a human.

10.   The method of claim 1, wherein the KCNQ channel is a heteromeric channel.

11.   The method of claim 1, wherein the KCNQ channel is a homomeric channel.

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1   12. The method of claim 10, wherein the heteromeric KCNQ channel
2 comprises a KCNQ2 polypeptide subunit.

1   13. The method of claim 10, wherein the heteromeric KCNQ channel
2 comprises a KCNQ3 polypeptide subunit.

1   14. The method of claim 12, wherein the KCNQ channel is KCNQ2/3.

1   15. The method of claim 1, wherein the potassium channel-opening
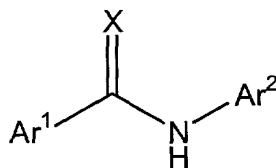2 amount is 0.1 mg/kg to 200 mg/kg.

1   16. The method of claim 15, wherein the potassium channel-opening
2 amount is 10 mg/kg to 100 mg/kg.

1   17. The method of claim 1, wherein the composition is administered
2 orally.

1   18. The method of claim 1, wherein the composition is administered by
2 injection.

1   19. The method of claim 1, wherein the composition is administered
2 after a surgical procedure.

1   20. The method of claim 1, wherein the compound able to increase ion
2 flow through KCNQ potassium channels has the formula:

3
4 wherein
5   Ar^1 and Ar^2 are each members independently selected from the group
6   consisting of aryl, substituted aryl, heteroaryl and substituted
7   heteroaryl; and
8   X is a member selected from the group consisting of O, S and $N\text{-}R^1$,
9   wherein R^1 is a member selected from the group consisting of H, $(C_1$-
10      $C_8)$alkyl, substituted $(C_1\text{-}C_8)$alkyl, aryl, substituted aryl, heteroaryl,

11   substituted heteroaryl, aryl(C_1-C_4)alkyl, substituted aryl$(C_1-$

12   C_4)alkyl, CN, -C(O)R^2, -OR^3, -C(O)NR^3R^4, and -S(O)$_2$NR^3R^4;

13   wherein R^2 is a member selected from the group consisting of $(C_1-$

14   C_8)alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl,

15   heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl and

16   substituted aryl(C_1-C_4)alkyl; and

17   R^3 and R^4 are each members independently selected from the group

18 consisting of hydrogen, (C_1-C_8)alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl,

19 heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl and substituted aryl(C_1-C_4)alkyl, or R^3

20 and R^4 can be combined with the nitrogen to which each is attached to form a 5-, 6- or 7-

21 membered ring optionally having additional heteroatoms at the ring vertices.

1   21.   The method according to claim 20, wherein Ar^1 is a member

2 selected from the group consisting of phenyl, substituted phenyl, indolyl, substituted

3 indolyl, benzofuranyl, substituted benzofuranyl, furanyl, substituted furanyl, thienyl,

4 substituted thienyl, isothiazolyl, substituted isothiazolyl, pyrazolyl and substituted

5 pyrazolyl.

1   22.   The method according to claim 20, wherein Ar^1 is substituted

2 phenyl, substituted or unsubstituted 2-indolyl and substituted or unsubstituted 2-thienyl.

1   23.   The method according to claim 20, wherein X is O.

1   24.   The method according to claim 22, wherein the Ar^1 substituents are

2 selected from the group consisting of halogen, alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy,

3 halo(C_1-C_4)alkoxy, nitro, cyano, -NHC(O)R^7, -NHR^7, phenyl and substituted phenyl,

4 wherein

5   R^7 is a member selected from hydrogen, (C_1-C_8)alkyl, substituted

6 (C_1-C_8)alkyl, cycloalkyl, substituted cycloalkyl, heteroalkyl, substituted heteroalkyl,

7 heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, heteroaryl, substituted

8 heteroaryl, aryl(C_1-C_4)alkyl and substituted aryl(C_1-C_4)alkyl, or R^7 can be combined with

9 the nitrogen to which it is attached to form a 5-, 6- or 7-membered ring optionally having

10 additional heteroatoms at the ring vertices.

1   25.   The method according to claim 20, wherein Ar^2 is selected from

2 the group consisting of heteroaryl and substituted heteroaryl.

38

1   26.   The method according to claim 20, wherein Ar^1 is substituted aryl;

2 Ar^2 is heteroaryl or substituted heteroaryl; and X is O.

1   27.   The method according to claim 24, wherein Ar^2 is pyridyl or

2 substituted pyridyl.

1   28.   The method according to claim 27, wherein Ar^2 is selected from

2 the group consisting of 6-methyl-3-pyridyl and 2-chloro-5-pyridyl.

1   29.   The method according to claim 27, wherein Ar^1 is substituted

2 phenyl.

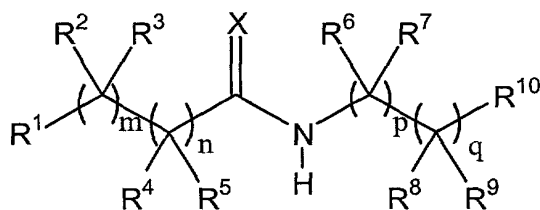1   30.   The method according to claim 29, said compound having the
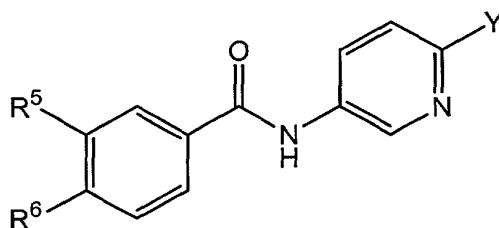
2 formula:

3

4   wherein,

5   Y is a member selected from the group consisting of halogen, C_1-C_4 alkyl,

6 C_1-C_4 substituted alkyl, $-OCH_3$ and $-OCF_3$, and R^5 and R^6 are members independently

7 selected from the group consisting of H, halogen, alkyl, halo(C_1-C_4)alkyl, nitro, cyano

8 and phenyl, with the proviso that both R^5 and R^6 are not H.

1   31.   The method according to claim 30, wherein R^5 and R^6 are members

2 independently selected from the group consisting of H, F, and Cl, with the proviso that

3 both R^5 and R^6 are not H.

1   32.   The method of claim 1, wherein the compound able to increase ion

2 flow through KCNQ potassium channels has the formula:

3

4 wherein

5   R^1 is a member selected from the group consisting of substituted or

6   unsubstituted branched (C_3-C_8)alkyl, substituted or unsubstituted

7   (C_3-C_8)cycloalkyl, substituted or unsubstituted $(C_3-$

8      $C_8)$heterocycloalkyl, substituted or unsubstituted aryl and

9   substituted or unsubstituted heteroaryl;

10   R^2, R^3, R^4 and R^5 are each members independently selected from the group

11   consisting of hydrogen, fluorine and substituted or unsubstituted

12   (C_1-C_8)alkyl, or optionally any two of R^2, R^3, R^4 and R^5 are joined

13   together to form a three- to seven-membered ring, having from 0 to

14   3 heteroatoms as ring members, or R^2 and R^4 taken together form a

15   second bond between the carbon atoms to which each is attached,

16   or R^2, R^3, R^4 and R^5 taken together represent a second and third

17   bond between the carbon atoms to which each is attached;

18   R^6, R^7, R^8 and R^9 are each members independently selected from the group

19   consisting of hydrogen, fluorine and substituted or unsubstituted

20   (C_1-C_8)alkyl, or optionally any two of R^6, R^7, R^8 and R^9 are joined

21   together to form a three- to seven-membered ring, having from 0 to

22   3 heteroatoms as ring members;

23   R^{10} is a member selected from the group consisting of substituted or

24   unsubstituted (C_3-C_8)cycloalkyl, substituted or unsubstituted $(C_3-$

25      $C_8)$heterocycloalkyl, substituted or unsubstituted aryl and

26   substituted or unsubstituted heteroaryl;

27   X is a member selected from the group consisting of O, S and N-R^{11},

28   wherein R^{11} is a member selected from the group consisting of H, $(C_1-$

29        $C_8)$alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl,

30   heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl, substituted

31   aryl(C_1-C_4)alkyl, -CN, -C(O)R^{12}, -OR^{13}, -NR^{13}R^{14},

32   -C(O)NR^{13}R^{14}, and -S(O)$_2$NR^{13}R^{14};

33   wherein R^{12} is a member selected from the group consisting of $(C_1-$

34        $C_8)$alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl,

35   heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl and

36   substituted aryl(C_1-C_4)alkyl; and

40

37   R^{13} and R^{14} are each members independently selected from the

38   group consisting of hydrogen, (C_1-C_8)alkyl, substituted $(C_1-$

39 $C_8)$alkyl, aryl, substituted aryl, heteroaryl, substituted

40   heteroaryl, aryl(C_1-C_4)alkyl and substituted aryl$(C_1-$

41 $C_4)$alkyl, or R^{13} and R^{14} can be combined with the nitrogen

42   to which each is attached to form a 5-, 6- or 7-membered

43   ring optionally having additional heteroatoms at the ring

44   vertices; and

45   m, n, p and q are each independently an integer of from 0 to 1, with the

46   proviso that at least one of m, n, p or q is 1.

1   33.   The method of claim 32, wherein X of the compound is O.

1   34.   The method of claim 32, wherein m and n of the compound are

2   zero.

1   35.   The method of claim 32, wherein m of the compound is 1 and n of

2   the compound is zero.

1   36.   The method of claim 32, wherein m and n of the compound are

2   each 1.

1   37.   The method of claim 32, wherein m and p of the compound are

2   each zero, and n and q of the compound are each 1.

1   38.   The method of claim 32, wherein m, n, p and q of the compound

2   are each 1.

1   39.   The method of claim 32, wherein R^2 and R^4 of the compound,

2   taken together, form a second bond joining the carbon atoms to which each is attached.

1   40.   The method of claim 32, wherein m and p of the compound are

2   each 1, R^2, R^3, R^6 and R^7 of the compound are each hydrogen, n and q of the compound

3   are each zero, and R^{10} of the compound is selected from the group consisting of

4   substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.

41

1   41.   The method of claim 40, wherein R^{10} of the compound is

2   substituted aryl having from one to three substituents selected from the group consisting

3   of halogen, halo(C_1-C_4)alkyl, halo(C_1-C_4)alkoxy, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, nitro,

4   cyano, phenyl and methylenedioxy.

1   42.   The method of claim 32, wherein m, n, p and q of the compound

2   are each 1, and R^2, R^3, R^4, R^5, R^6, R^7, R^8 and R^9 of the compound are each hydrogen.

1   43.   The method of claim 32, wherein m, n, p and q of the compound

2   are each 1; R^2, R^3, R^4, R^5, R^6, R^7, R^8 and R^9 of the compound are each hydrogen; and R^{10}

3   of the compound is selected from the group consisting of substituted or unsubstituted aryl

4   and substituted or unsubstituted heteroaryl.

1   44.   The method of claim 43, wherein R^1 of the compound is selected

2   from the group consisting of substituted or unsubstituted branched (C_3-C_8)alkyl, and

3   substituted or unsubstituted (C_3-C_8)cycloalkyl.

1   45.   A method for reducing anxiety in a subject in need thereof by

2   increasing ion flow through KCNQ potassium channels in a cell, the method comprising

3   the step of administering to the subject a pharmaceutical composition comprising a

4   pharmaceutically acceptable carrier and a compound able to increase ion flow through

5   KCNQ potassium channels, said composition administered to the subject in a potassium

6   channel-opening amount, thereby reducing anxiety in the subject.

1   46.   The method of claim 45, wherein the anxiety is caused by panic

2   disorder, generalized anxiety disorder, or stress disorder.

1   47.   The method of claim 46, wherein the stress disorder is acute stress

2   disorder or post-traumatic stress disorder.

1   48.   The method of claim 45, wherein the subject is a human.

1   49.   The method of claim 45, wherein the KCNQ channel is a

2   heteromeric channel.

1   50.   The method of claim 45, wherein the KCNQ channel is a

2   homomeric channel.

1   51.   The method of claim 50, wherein the heteromeric KCNQ channel

2 comprises a KCNQ2 polypeptide subunit.

1   52.   The method of claim 50, wherein the heteromeric KCNQ channel

2 comprises a KCNQ3 polypeptide subunit.

1   53.   The method of claim 52, wherein the KCNQ channel is KCNQ2/3.
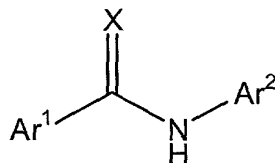
1   54.   The method of claim 45, wherein the potassium channel-opening

2 amount is 0.1 mg/kg to 200 mg/kg.

1   55.   The method of claim 54, wherein the potassium channel-opening

2 amount is 10 mg/kg to 100 mg/kg.

1   56.   The method of claim 45, wherein the composition is administered

2 orally.

1   57.   The method of claim 45, wherein the composition is administered

2 by injection.

1   58.   The method of claim 45, wherein the compound able to increase

2 ion flow through KCNQ potassium channels has the formula:

$$\mathrm{Ar^1}-\overset{\displaystyle \overset{X}{\|}}{\mathrm{C}}-\underset{\underset{\displaystyle H}{|}}{\mathrm{N}}-\mathrm{Ar^2}$$

3

4   wherein

5   Ar^1 and Ar^2 are each members independently selected from the group

6   consisting of aryl, substituted aryl, heteroaryl and substituted

7   heteroaryl; and

8   X is a member selected from the group consisting of O, S and N-R^1,

9   wherein R^1 is a member selected from the group consisting of H, (C_1-

10   C_8)alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl, heteroaryl,

11   substituted heteroaryl, aryl(C_1-C_4)alkyl, substituted aryl(C_1-

12   C_4)alkyl, CN, -C(O)R^2, -OR^3, -C(O)NR^3R^4, and -S(O)$_2$NR^3R^4;

43

13	wherein R^2 is a member selected from the group consisting of $(C_1-$
14	$C_8)$alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl,
15	heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl and
16	substituted aryl(C_1-C_4)alkyl; and
17	R^3 and R^4 are each members independently selected from the group
18	consisting of hydrogen, (C_1-C_8)alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl,
19	heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl and substituted aryl(C_1-C_4)alkyl, or R^3
20	and R^4 can be combined with the nitrogen to which each is attached to form a 5-, 6- or 7-
21	membered ring optionally having additional heteroatoms at the ring vertices.

1	59. The method according to claim 58, wherein Ar^1 is a member
2	selected from the group consisting of phenyl, substituted phenyl, indolyl, substituted
3	indolyl, benzofuranyl, substituted benzofuranyl, furanyl, substituted furanyl, thienyl,
4	substituted thienyl, isothiazolyl, substituted isothiazolyl, pyrazolyl and substituted
5	pyrazolyl.

| 1 | 60. The method according to claim 58, wherein Ar^1 is substituted |
| 2 | phenyl, substituted or unsubstituted 2-indolyl and substituted or unsubstituted 2-thienyl. |

| 1 | 61. The method according to claim 58, wherein X is O. |

1	62. The method according to claim 60, wherein the Ar^1 substituents are
2	selected from the group consisting of halogen, alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy,
3	halo(C_1-C_4)alkoxy, nitro, cyano, -NHC(O)R^7, -NHR^7, phenyl and substituted phenyl,
4	wherein
5	R^7 is a member selected from hydrogen, (C_1-C_8)alkyl, substituted
6	(C_1-C_8)alkyl, cycloalkyl, substituted cycloalkyl, heteroalkyl, substituted heteroalkyl,
7	heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, heteroaryl, substituted
8	heteroaryl, aryl(C_1-C_4)alkyl and substituted aryl(C_1-C_4)alkyl, or R^7 can be combined with
9	the nitrogen to which it is attached to form a 5-, 6- or 7-membered ring optionally having
10	additional heteroatoms at the ring vertices.

| 1 | 63. The method according to claim 58, wherein Ar^2 is selected from |
| 2 | the group consisting of heteroaryl and substituted heteroaryl. |

44

1   64.   The method according to claim 58, wherein Ar^1 is substituted aryl;

2   Ar^2 is heteroaryl or substituted heteroaryl; and X is O.

1   65.   The method according to claim 62, wherein Ar^2 is pyridyl or

2   substituted pyridyl.

1   66.   The method according to claim 65, wherein Ar^2 is selected from

2   the group consisting of 6-methyl-3-pyridyl and 2-chloro-5-pyridyl.

1   67.   The method according to claim 65, wherein Ar^1 is substituted

2   phenyl.

1   68.   The method according to claim 67, said compound having the
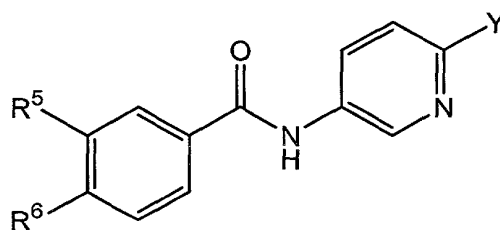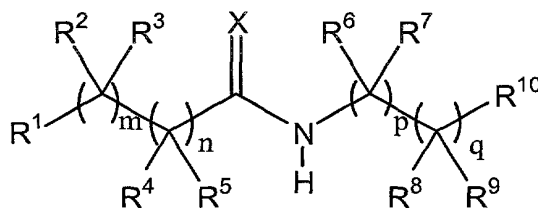
2   formula:

3

4   wherein,

5   Y is a member selected from the group consisting of halogen, C_1-C_4 alkyl,

6   C_1-C_4 substituted alkyl, -OCH_3 and -OCF_3, and R^5 and R^6 are members independently

7   selected from the group consisting of H, halogen, alkyl, halo(C_1-C_4)alkyl, nitro, cyano

8   and phenyl, with the proviso that both R^5 and R^6 are not H.

1   69.   The method according to claim 68, wherein R^5 and R^6 are members

2   independently selected from the group consisting of H, F, and Cl, with the proviso that

3   both R^5 and R^6 are not H.

1   70.   The method of claim 45, wherein the compound able to increase

2   ion flow through KCNQ potassium channels has the formula:

3

45

4   wherein

5   R^1 is a member selected from the group consisting of substituted or

6   unsubstituted branched (C_3-C_8)alkyl, substituted or unsubstituted

7   (C_3-C_8)cycloalkyl, substituted or unsubstituted $(C_3-$

8     $C_8)$heterocycloalkyl, substituted or unsubstituted aryl and

9   substituted or unsubstituted heteroaryl;

10   R^2, R^3, R^4 and R^5 are each members independently selected from the group

11   consisting of hydrogen, fluorine and substituted or unsubstituted

12   (C_1-C_8)alkyl, or optionally any two of R^2, R^3, R^4 and R^5 are joined

13   together to form a three- to seven-membered ring, having from 0 to

14   3 heteroatoms as ring members, or R^2 and R^4 taken together form a

15   second bond between the carbon atoms to which each is attached,

16   or R^2, R^3, R^4 and R^5 taken together represent a second and third

17   bond between the carbon atoms to which each is attached;

18   R^6, R^7, R^8 and R^9 are each members independently selected from the group

19   consisting of hydrogen, fluorine and substituted or unsubstituted

20   (C_1-C_8)alkyl, or optionally any two of R^6, R^7, R^8 and R^9 are joined

21   together to form a three- to seven-membered ring, having from 0 to

22   3 heteroatoms as ring members;

23   R^{10} is a member selected from the group consisting of substituted or

24   unsubstituted (C_3-C_8)cycloalkyl, substituted or unsubstituted $(C_3-$

25    $C_8)$heterocycloalkyl, substituted or unsubstituted aryl and

26   substituted or unsubstituted heteroaryl;

27   X is a member selected from the group consisting of O, S and N-R^{11},

28   wherein R^{11} is a member selected from the group consisting of H, $(C_1-$

29    $C_8)$alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl,

30   heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl, substituted

31   aryl(C_1-C_4)alkyl, -CN, -C(O)R^{12}, -OR^{13}, -N$R^{13}R^{14}$,

32   -C(O)N$R^{13}R^{14}$, and -S(O)$_2$N$R^{13}R^{14}$;

33   wherein R^{12} is a member selected from the group consisting of $(C_1-$

34    $C_8)$alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl,

35   heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl and

36   substituted aryl(C_1-C_4)alkyl; and

46

37   R^{13} and R^{14} are each members independently selected from the

38   group consisting of hydrogen, (C_1-C_8)alkyl, substituted $(C_1-$

39   C_8)alkyl, aryl, substituted aryl, heteroaryl, substituted

40   heteroaryl, aryl(C_1-C_4)alkyl and substituted aryl$(C_1-$

41   C_4)alkyl, or R^{13} and R^{14} can be combined with the nitrogen

42   to which each is attached to form a 5-, 6- or 7-membered

43   ring optionally having additional heteroatoms at the ring

44   vertices; and

45   m, n, p and q are each independently an integer of from 0 to 1, with the

46 proviso that at least one of m, n, p or q is 1.

1   71.   The method of claim 70, wherein X of the compound is O.

1   72.   The method of claim 70, wherein m and n of the compound are

2 zero.

1   73.   The method of claim 70, wherein m of the compound is 1 and n of

2 the compound is zero.

1   74.   The method of claim 70, wherein m and n of the compound are

2 each 1.

1   75.   The method of claim 70, wherein m and p of the compound are

2 each zero, and n and q of the compound are each 1.

1   76.   The method of claim 70, wherein m, n, p and q of the compound

2 are each 1.

1   77.   The method of claim 70, wherein R^2 and R^4 of the compound,

2 taken together, form a second bond joining the carbon atoms to which each is attached.

1   78.   The method of claim 70, wherein m and p of the compound are

2 each 1, R^2, R^3, R^6 and R^7 of the compound are each hydrogen, n and q of the compound

3 are each zero, and R^{10} of the compound is selected from the group consisting of

4 substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.

1   79.   The method of claim 78, wherein R^{10} of the compound is

2   substituted aryl having from one to three substituents selected from the group consisting

3   of halogen, halo(C_1-C_4)alkyl, halo(C_1-C_4)alkoxy, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, nitro,

4   cyano, phenyl and methylenedioxy.

1   80.   The method of claim 70, wherein m, n, p and q of the compound

2   are each 1, and R^2, R^3, R^4, R^5, R^6, R^7, R^8 and R^9 of the compound are each hydrogen.

1   81.   The method of claim 70, wherein m, n, p and q of the compound

2   are each 1; R^2, R^3, R^4, R^5, R^6, R^7, R^8 and R^9 of the compound are each hydrogen; and R^{10}

3   of the compound is selected from the group consisting of substituted or unsubstituted aryl

4   and substituted or unsubstituted heteroaryl.

1   82.   The method of claim 81, wherein R^1 of the compound is selected

2   from the group consisting of substituted or unsubstituted branched (C_3-C_8)alkyl, and

3   substituted or unsubstituted (C_3-C_8)cycloalkyl.